Claims

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What is claimed is:

1. A composition comprising first and second nucleic acid sequences, wherein said first nucleic acid sequence is a truncated A subunit coding region obtained or derived from a bacterial ADP-ribosylating exotoxin, and said second nucleic acid sequence is a truncated B subunit coding region obtained or derived from a bacterial ADP-ribosylating exotoxin, with the proviso that each of said truncated subunit coding regions has a 5' deletion and encodes a subunit peptide not having an amino terminal bacterial signal peptide.

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2. The composition of claim 1, wherein said first and second nucleic acid sequences are present in a single nucleic acid construct.

3. The composition of claim 2, wherein said nucleic acid construct is a plasmid vector.

4. The composition of claim 2, wherein the first and second nucleic acid sequences are operably linked to a transcriptional control element.

5. The composition of claim 4, wherein said transcriptional control element is a heterologous promoter.

6. The composition of claim 1 wherein said first and second nucleic acid sequences are present in separate nucleic acid constructs.

7. The composition of claim 6, wherein said separate nucleic acid constructs are plasmid vectors.

8. The composition of claim 1, wherein the truncated subunit coding regions are obtained or derived from the same bacterial ADP-ribosylating exotoxin.

9. The composition of claim 8, wherein said bacterial ADP-ribosylating exotoxin is a cholera toxin (CT).

10. The composition of claim 8, wherein said bacterial ADP-ribosylating exotoxin is an *E. coli* heat labile enterotoxin (LT).

11. The composition of claim 1, wherein at least one of the truncated subunit coding regions has been genetically modified to detoxify the subunit peptide encoded thereby.

12. The composition of claim 11, wherein the truncated A subunit coding region has been genetically modified to disrupt or inactivate ADP-ribosyl transferase activity in the subunit peptide encoded thereby.

13. The composition of claim 1, wherein the truncated A subunit coding region has been further genetically modified so as to delete a C-terminal KDEL or RDEL motif in the subunit peptide encoded thereby.

14. The composition of claim 1 further comprising an antigen of interest.

15. The composition of claim 14, wherein said antigen is from a bacterial, viral or parasitic pathogen.

16. The composition of claim 1, further comprising a third nucleic acid sequence that encodes an antigen of interest.

17. The composition of claim 16, wherein said antigen is from a bacterial, viral or parasitic pathogen.

18. The composition of claim 16, wherein said third nucleic acid sequence is present in a nucleic acid construct that does not contain said first or said second nucleic acid sequence.

19. The composition of claim 18, wherein the nucleic acid construct containing the third nucleic acid sequence is a plasmid vector.

20. The composition of claim 16, wherein said third nucleic acid sequence is present in a nucleic acid construct that also contains at least one of said first or said second nucleic acid sequence.

21. The composition of claim 20, wherein the nucleic acid construct containing the third nucleic acid sequence is a plasmid vector.

22. The composition of claim 1, wherein said composition is in a particulate form.

23. The composition of claim 22, wherein said particulate composition is suitable for transdermal delivery via a particle delivery device.

24. The composition of claim 1, further comprising a pharmaceutically acceptable vehicle or excipient.

25. The composition of claim 1, wherein the first and second nucleic acid sequences are coated onto a core carrier particle.

26. The composition of claim 25, wherein the core carrier particle has an average diameter of about 0.1 to about 10μm.

27. The composition of claim 25, wherein the core carrier particle comprises a metal.

28. The composition of claim 27 wherein the metal is gold.

29. The composition of claim 28 wherein the core carrier particle has a diameter of about 1 to about 3 μm.

30. The composition of claim 1 further comprising a transfection facilitating agent.

31. The composition of claim 30, wherein the transfection facilitating agent is a liposome.

32. A composition comprising first and second nucleic acid sequences, wherein said first nucleic acid sequence is a modified A subunit coding region obtained or derived from a bacterial ADP-ribosylating exotoxin, and said second nucleic acid sequence is a B subunit coding region obtained or derived from a bacterial ADP-ribosylating exotoxin, with the proviso that said modified A subunit coding region and said B subunit coding region each encode a mature subunit peptide, and with the further proviso that the modified A subunit coding region has been genetically modified so as to delete a C-terminal KDEL or RDEL motif in the subunit peptide encoded thereby.

33. The composition of claim 32, wherein said first and second nucleic acid sequences are present in a single nucleic acid construct.

34. The composition of claim 33, wherein said nucleic acid construct is a plasmid vector.

35. The composition of claim 33, wherein the first and second nucleic acid sequences are operably linked to a transcriptional control element.

36. The composition of claim 35, wherein said transcriptional control element is a heterologous promoter.

37. The composition of claim 32, wherein said first and second nucleic acid sequences are present in separate nucleic acid constructs.

38. The composition of claim 37, wherein said separate nucleic acid constructs are plasmid vectors.

39. The composition of claim 32, wherein the B and modified A subunit coding regions are obtained or derived from the same bacterial ADP-ribosylating exotoxin.

40. The composition of claim 39, wherein said bacterial ADP-ribosylating exotoxin is a cholera toxin (CT).

41. The composition of claim 39, wherein said bacterial ADP-ribosylating exotoxin is an *E. coli* heat labile enterotoxin (LT).

42. The composition of claim 32, wherein at least one of the B or modified A subunit coding regions has been genetically modified to detoxify the subunit peptide encoded thereby.

43. The composition of claim 42, wherein the modified A subunit coding region has been genetically modified to disrupt or inactivate ADP-ribosyl transferase activity in the subunit peptide encoded thereby.

44. The composition of claim 32, wherein the modified A subunit coding region and the B subunit coding region have each been truncated by a 5' deletion whereby each of said truncated subunit coding regions encodes a subunit peptide not having an amino terminal bacterial signal peptide.

45. The composition of claim 32 further comprising an antigen of interest.

46. The composition of claim 45, wherein said antigen is from a bacterial, viral or parasitic pathogen.

47. The composition of claim 32 further comprising a third nucleic acid sequence that encodes an antigen of interest.

48. The composition of claim 47, wherein said antigen is from a bacterial, viral or parasitic pathogen.

49. The composition of claim 47, wherein said third nucleic acid sequence is present in a nucleic acid construct that does not contain said first or said second nucleic acid sequence.

50. The composition of claim 49, wherein the nucleic acid construct containing the third nucleic acid sequence is a plasmid vector.

51. The composition of claim 47, wherein said third nucleic acid sequence is present in a nucleic acid construct that also contains at least one of said first or said second nucleic acid sequence.

52. The composition of claim 51, wherein the nucleic acid construct containing the third nucleic acid sequence is a plasmid vector.

53. The composition of claim 32, wherein said composition is in a particulate form.

54. The composition of claim 53, wherein said particulate composition is suitable for transdermal delivery via a particle delivery device.

55. The composition of claim 32 further comprising a pharmaceutically acceptable vehicle or excipient.

56. A composition according to claim 55, wherein the first and second nucleic acid sequences are coated onto a core carrier particle.

57. The composition of claim 56, wherein the core carrier particle has an average diameter of about 0.1 to about 10μm.

58. The composition of claim 56, wherein the core carrier particle comprises a metal.

59. The composition of claim 58, wherein the metal is gold.

60. The composition of claim 59 wherein the core carrier particle has a diameter of about 1 to about 3 μm.

61. The composition of claim 32 further comprising a transfection facilitating agent.

62. The composition of claim 61, wherein the transfection facilitating agent is a liposome.

63. A method for enhancing an immune response against an antigen of interest in a vertebrate subject, the method comprising:

DETAILED ACTION

Restriction to one of the following inventions is required under 35 U.S.C. 121:

1. Claims 1-62, drawn to compositions comprising first and second nucleic acids sequences encoding truncated A and B subunit coding regions obtained or derived from a bacterial ADP-ribosylating exotoxin, wherein each coding region has a 5' deletion and fails to encode an amino terminal bacterial signal peptide, classified in class 536, subclass 23.7.
2. Claims 63-80, drawn to methods of enhancing an immune response, classified in class 514, subclass 44

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the composition could be used for purposes other than enhancing an immune response, such as studying the structure and function of the encoded A and B subunits. The compositions could be used to deliver expression vectors to expression systems *in vitro* for production of the encoded proteins for subsequent physical and kinetic characterization.

Because these inventions are distinct for the reasons given above, have acquired a separate status in the art as shown by their different classification and their

recognized divergent subject matter, and because each invention requires a separate, non-coextensive search, restriction for examination purposes as indicated is proper.

Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(l).

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 103-306-5441. The examiner can normally be reached Monday through Friday between the hours of 6:20 AM and 3:50 PM. The examiner is off on alternate Fridays, but is usually in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John Leguyader, can be reached at 703-308-0447. The official central fax number is 703-872-9306. Inquiries of a general nature or relating to the status of the application should be directed to the Patent Analyst Trina Turner whose telephone number is 703-305-3413.

DAVE T. NGUYEN
PRIMARY EXAMINER

Richard Schnizer, Ph.D.